**INTRODUCTION**

Previous *ex vivo* studies show that diffusion tensor imaging (DTI) is useful in assessing axonal and myelin degeneration in the peripheral nervous system (PNS). However, the sensitivity of DTI in assessing peripheral nerve regeneration *in vivo* remains unclear. In the present study, we performed *in vivo* DTI and morphological analyses at multiple time points during a four-week period after nerve injury to examine degeneration and regeneration in the rat PNS.

**MATERIALS AND METHODS**

**Animal models**

For MRI, 16 rats were randomly divided into two groups: group P (permanently crushed; n = 7) and group T (temporarily crushed; n = 9). In both groups, the right sciatic nerve was exposed and ligated at the proximal-thigh level with a 3-0 silk to produce a crush injury. For histological analyses, 30 rats were used: group P (n = 15) and group T (n = 15). To compare the DTI with histological changes, samples were collected at pre-injured time and at 1, 2, 3 and 4 weeks after the crush injury in both groups.

**MRI**

Rats were anesthetized with a mixture of oxygen and isoflurane. The right leg was stretched and immobilized by a custom-made holder. Serial MRI of the right leg on each rat was performed before the operation (defined as 0 weeks), and then performed at the time points of 1, 2, 3 and 4 weeks after the crush injury. MRI was performed in a horizontal 4.7 Tesla magnet (Bruker Biospec, Germany). The MRI protocol included echo-planar imaging (EPI) for DTI. Transverse slices from a rat’s sciatic nerve were collected from 2 mm proximal to 10 mm distal to the lesion site. The total imaging time was 32 min for each session.

**DTI data analyses**

The resulting tensor element maps were used to derive the eigenvalues of the tensor (\(\lambda_1, \lambda_2,\) and \(\lambda_3\)) by matrix diagonalization. The quantitative indices were derived using MR Vision software (MR Vision Inc, Winchester, MA, USA). Regions of interest (ROI) in the lesion were defined on the T2WI based on the anatomic knowledge about the location of the sciatic nerve. The parameters of FA, \(\lambda_1\), and \(\lambda_2\) were calculated by the following equations. The T2W signal intensity was also calculated.

**Histological analyses**

To identify the histological differences in the injured sciatic nerves, we examined cross sections of sciatic nerves by using light microscopy. Semithin transverse sections of 2 \(\mu m\) thickness were collected onto glass slides and stained with toluidine blue. For quantitative analysis, myelinated axon profiles were counted using the automatic threshold tool. In each image (area: \(1.29 \times 10^5\mu m^2\)), we calculated the number of axons per \(mm^2\) (\(N/mm^2\)) and the ratio of myelinated axon areas in the field, which was expressed as a percentage (%).

**RESULTS**

**DTI**

The representative apparent diffusion coefficient (ADC) maps and T2WI from group T are shown in Fig. 1. In the transverse sections, degenerative and regenerative changes in the peripheral nerves were most clearly visible 4 mm distal to the injury site. Time course of FA (2A), \(\lambda_1\) (2B), and \(\lambda_3\) (2C) in the lesion, which is 4 mm distal to the crush site, are shown in Fig. 2. The FA decreases immediately post injury in both groups, but subsequently increases in group T at 3 and 4 weeks post injury (with the week 4 value significantly higher). The \(\lambda_2\) in group T is significantly lower than that of group P at 3 weeks post injury. This was followed by a complete disappearance at 3 weeks post injury. In group T, the number of axons and the ratio of myelinated areas were decreased at 1 and 2 weeks, but were increased at 3 and 4 weeks post injury, as regeneration proceeded.

**DISCUSSION**

This study investigated the sensitivity of DTI in detecting peripheral nerve degeneration and regeneration *in vivo*. Our results demonstrated that decreased FA and increased \(\lambda_2\) were observed in the degenerative phase, and that increased FA and decreased \(\lambda_2\) were observed in the regenerative phase. Furthermore, the changes in FA and \(\lambda_2\) were strongly correlated with histological changes, including axonal and myelin regeneration. The axial diffusivity, \(\lambda_2\), on the other hand, failed to show significant pre- and post-crush injury changes.

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**Fig. 1**

**Fig. 2**

**Fig. 3**

**Fig. 4**

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